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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/469,197	12/21/99	PORTNOY D	B98-039-2

HM22/1121

SCIENCE & TECHNOLOGY LAW GROUP
75 DENISE DRIVE
HILLSBOUROUGH CA 94010

EXAMINER	
LACOURCIERE,K	
ART UNIT	**PAPER NUMBER**
1635	7

DATE MAILED: 11/21/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

FILE

Office Action Summary

Application No.	Applicant(s)
09/469,197	Portney et al.
Examiner	**Group Art Unit**
Karen A. Lacourciere	1635

☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *11-65* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *11, 17, 20, 26, and 40-65* is/are rejected.

☒ Claim(s) *12-16, 18, 19, 21-25, and 27-39* is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

F/CE

DETAILED ACTION

Terminal Disclaimer

The terminal disclaimer filed on 10-31-2000 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of 6,004,815 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 11, 17, 20, 26, 40-43, 46 are rejected under 35 U.S.C. 102(a) as being anticipated by Dietrich et al.(reference cited on PTO form 1449, filed 2-16-00).

Dietrich et al. disclose a vaccine comprising an attenuated, non-virulent strain of Listeria monocytogenes wherein a foreign, non-secreted phage lysin is expressed and wherein the bacteria further comprises a plasmid encoding an antigen. The bacterium does not integrate into the host genome and is non-replicative. Dietrich et al. disclose a method of inducing an immune response using their vaccine, which would further qualify their vaccine as a pharmaceutical composition. Therefore, Dietrich et al. anticipates claims 11, 17, 20, 26, 40-43 and 46.

Claim Rejections - 35 USC § 112

Claims 40-65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 40-65 are indefinite because they are drawn to methods which do not comprise a method step which relates back to the goal set forth by the preamble of the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 53-65 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of reducing breast tumor size using the claimed bacterium to introduce a BRCA1 antigen, does not reasonably provide enablement for generally treating any disease by delivering a foreign antigen . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The following factors have been considered in formulating this rejection (*In re Wands*, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or

unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

Claims 53-64 are drawn to a method of treating a disease wherein a therapeutic agent is delivered to a cell using a non-virulent bacterium which comprises a foreign, non-secreted, expressed cytolysin.

The specification provides one example wherein an E.coli expressing LLO is used to deliver a truncated BRAC1 antigen to breast tumors when injected directly into the tumor, with a resultant reduction in tumor size. Further, the specification provides examples wherein various strains of bacteria, expressing various cyolysins, are used to deliver various foreign antigens into cells.

The claims are drawn broadly to treating any disease using a non-virulent bacterium to deliver any therapeutic agent. The claims read on delivery of any therapeutic agent, including therapeutic agents like gene therapy vectors and antisense, and require a therapeutic, treatment effect to be realized by these methods.

The specification has not provided any guidance which would direct one skilled in the art to determine what therapeutic agent can be delivered by these methods to treat a particular disease. Although the specification provides examples wherein foreign antigens are delivered into cells, there is no evidence to indicate that the delivery is at a concentration effective enough to elicit a treatment effect, as required by the claimed methods, nor is there any guidance as to what antigen will provide a therapeutic effect for a particular disease. The claimed methods would

encompass antisense and gene therapy methods which are well known in the art to be highly unpredictable, due mainly to delivery issues and, in the case of gene therapy, for problems with sustainable gene expression (see for example Branch and Anderson). The specification demonstrates delivery of nucleic acid constructs to the cytosol of various cells, however there is no evidence that these nucleic acid constructs are delivered specifically to a target cell in a concentration effective to result in a treatment effect, as required by the claimed methods. Further, in the case of gene therapy, the specification provides no guidance which would solve other major hurdles to *in vivo* gene therapy treatment methods, for example, the unpredictable loss of expression of a therapeutic gene. The specification does not provide any guidance such that one skilled in the art could delivery a vector specifically to a target cell such that sufficient and sustained expression can be acheived, in a manner that would result in treatment for a disease. The determination of these factors would need to be done *de novo*, through undue trial and error experimentation, beyond what is taught in the specification, to allow one skilled in the art to practice the invention over the full scope claimed. Such undue trial and error experimentation would include the determination of what antigen or therapeutic agents can be specifically delivered to cells to treat a particular disease, what cells to target to treat a particular disease, how to deliver a concentration of antisense or gene therapy vectors to a target cell *in vivo* at a concentration effective to treat a particular disease, and what gene therapy vectors can be used to elicit sufficient and sustained expression of a therapeutic gene to result in a treatment effect for a particular disease.

Therefore, due to the broad breadth claimed, the level of unpredictability in the art, the lack of direction presented in the specification, the lack of working examples, and the quantity of experimentation required, one skilled in the art could not practice the methods of treatment claimed, over the full scope claimed, without undue trial and error experimention.

Claim Objections

Claims 12-16, 18, 19, 21-25, and 27-39 are objected to for being dependent on a rejected claim.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Lacourciere whose telephone number is (703) 308-7523.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached at (703) 308-0447. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SEAN MCGARRY
PATENT EXAMINER
TC 1600

Karen A. Lacourciere

November 20, 2000